The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HAIM AVIV, RAPHAEL BAR, MICHAEL SCHICKLER, and SHIMON AMSELEM

Appeal No. 2007-0092
Application No. 10/644,687

ON BRIEF

Before MILLS, GRIMES, and LINCK, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-10, 15-16 and 18-24.

Claim 1 reads as set forth in the Appendix attached to the Brief. Essentially, claim 1 is directed to a compound of formula I, having the (3S,4S) enantiomeric configuration and being in enantiomeric excess of at least 99.90% over the (3R,4R) enantiomer, or a pharmaceutically acceptable salt, ester or solvate of said compound.

The prior art cited by the examiner is:

Kloog et al. (Kloog)	5,284,867	Feb. 8, 1994
Mechoulam et al. (Mechoulam)	4,876,276	Oct. 24, 1989

References cited by Merits Panel:

Brewster et al. (Brewster), "Clinical pharmacokinetics of escalating i.v. doses of dexanabinol (HU-211), a neuroprotectant agent, in normal volunteers," Int. J. of Clin. Pharmacol., Vol. 35, No. 9, pp. 361-365 (1995)

Knoller et al. (Knoller), "Dexanabinol (HU-211) in the treatment of severe closed head injury: A randomized, placebo-controlled, phase II clinical trial," Crit. Care Med., Vol. 30, No.3, pp. 548-554 (2002)

Grounds of Rejection

Claims 1-10, 15-16 and 18-24 stand rejected under 35 U.S.C. § 102(b) over Kloog.

Claims 1-6 and 8-24 stand rejected under 35 U.S.C. § 103(a) over Kloog.

We reverse the anticipation and obviousness rejections. We enter four new grounds of rejection over Mechoulam, Brewster and Knoller.

DISCUSSION

Anticipation

Claims 1-10, 15-16 and 18-24 stand rejected under 35 U.S.C. § 102(b) over Kloog.

The standard under § 102 is one of strict identity. Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim. Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997). Every element of the claimed invention must be literally present,

arranged as in the claim. Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

According to the examiner (Answer, page 3), Kloog discloses

> the instantly claimed compound (HU-211), essentially free of the (3R,4R) enantiomer, various pharmaceutical formulations (compositions) for various types of administrations (columns 4-5) and methods of use for treating neurological disorders. The formulation is emulphor or emulsions and may contain antioxidants, preferably the antioxidant is α-tocopherol. See example 3, column 12, and colum 13, lines 1-5...
>
> The HU-211 compound obtained by the process of Mechoulam et al., and used by Kloog et al., (column 2, lines 23-41 of US '867) is obtained "in pure enantiomeric form." See US 4,876,276, column 2, lines 57-62. Therefore the phraseology "essentially free of the (3R,4R) enantiomer" is deemed (3S,4S) is in enantiomer excess of at least 99.90% over the (3R,4R) . . . .

We find the examiner has provided sufficient evidence to support a prima facie case of anticipation.

Where the prior art, as here, anticipates the claimed invention, the burden then falls on an appellant to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

Appellants put forth three Declarations as evidence that Kloog does not anticipate the pending claims. Appellants argue that "Claim 1 defines the dexanabinol as having the (3S,4S) configuration (Specification, page 6, lines 5-10) and being in enantiomeric excess of at least 99.90% over the (3R,4R) enantiomer (Specification, page 6, lines 10-

11), or a pharmaceutically acceptable salt, ester or solvate thereof (Specification, page 6, line 11)." Brief, page 3. Appellants argue that, "Kloog's HU-211 and the presently claimed high purity HU-211 are significantly different compounds with different properties, which are attributable to the differences in enantiomeric purity." Brief, page 4.

Appellants argue that the Mechoulam sample of dexanabinol having the (3S,4S) configuration is representative of the closest prior art because Kloog used the Mechoulam method to prepare the compound of interest. Brief, page 6.

According to Appellants, "[t]he Mechoulam sample was tested and found to contain 91.1% HU-211 and 0.26% HU-210, yielding an enantiomeric excess of 99.4%, which is less than the at least 99.90% claimed." Brief, page 6. The Appellants conclude that the difference between the claimed compound and that of Mechoulam and Kloog

> is much more than just the level of purity, as these compounds have significantly different properties. Kloog reports that ...HU-211 at about 25 mg/kg per body weight, administered most likely to mice, induced side effects such as stereotypy, locomoter hyperactivity and tachycardia. In contrast, the compound of interest of the present invention was administered at single doses of 50 mg/kg in rats, 25 mg/kg in rabbits and 50 mg/kg in monkeys with no observed adverse effects. This establishes that the presently claimed compounds are novel over the Kloog compound. [footnotes omitted]

Appellants further argue that the Declaration of Yacovan shows that when mice were administered their ultrapure sample of dexanabinol and the Mechoulam sample, the Mechoulam sample evidenced adverse effect in rectal temperature, spontaneous locomotion and catalepsy whereas the ultrapure sample did not. Brief, page 7.

Yacovan Declaration, paragraphs 7-9.

In response to appellants' arguments, the examiner again attributes the differences in purity to experimental error and/or design. Answer, page 7. The examiner further argues that Kloog states that their product was obtained "in pure enantiomeric form", and that the claim term "essentially" means "inherently free of the 3R,4R enantiomer." Answer, page 5. The examiner finds that appellants have "fail[ed] to provide any conclusive evidence that the HU-211 disclosed by Kloog et al., is not in enantiomeric excess of at least 99.90% over the (3R,4R) enantiomer." Id.

We agree, however, that appellants have provided persuasive evidence to rebut examiner's prima facie case of anticipation. In particular, Appellants' data in the Declaration of Bar reasonably establish that the difference in purity of the Mechoulam sample and that of the claimed dexanabinol is outside of the range of experimental error. Bar Declaration ¶ 8. The Declaration of Yacovan provides evidence that the properties of the compound of Mechoulam (as used in Kloog) are different from that of the claimed purity dexanabinol. Yacovan Declaration ¶ ¶ 8 and 9. Further the Mechoulam Declaration provides evidence that Kloog does not teach the claimed compound having the claimed enantiomeric excess. Mechoulam Declaration ¶ ¶ 9 and 10.

In view of the above, we find appellants have convincingly rebutted the examiner's prima facie case of anticipation and the rejection of the claims for anticipation is reversed.

35 U.S.C. § 103(a)

Claims 1-6 and 8-24 stand rejected under 35 U.S.C. § 103(a) over Kloog.

The examiner argues that "[e]ven if the claimed compound is substantially purer than the compound of Kloog et al., there must be new and novel properties, functions or utilities arising from the higher level of purity..." Answer, page 6. We do not entirely agree with this statement of the examiner. Appellant need only establish that the properties of the claimed purer compound are distinct and unexpected over of the compounds of Kloog and in view of the state of the art as understood by one of ordinary skill in the art.

The examiner has failed to provide evidence on the record before us that one of ordinary skill in the art would have expected the claimed purer compounds to have the reduced side effects and other properties evidenced in the Yacovan Declaration in view of the evidence of record and the state of the art. See, e.g., In re Skoner, 517 F.2d 947, 950, 186 USPQ 80, 82 (CCPA 1975).

In sum, we find the Declaration evidence and argument submitted by appellants would likewise overcome the rejection of claims 1-6 and 8-24 under 35 U.S.C. § 103(a) over Kloog. In particular, Appellants' data in the Declaration of Bar reasonably establishes that the difference in purity of the Mechoulam sample and that of the claimed dexanabinol is outside of the range of experimental error. Bar Declaration ¶ 8. The Declaration of Yacovan provides evidence that the properties of the compound of

Mechoulam (as used in Kloog) are different from that of the claimed purity dexanabinol. Yacovan Declaration ¶ ¶ 8 and 9. Further, the Mechoulam Declaration provides evidence that Kloog does not teach the claimed compound having the claimed enantiomeric excess. Mechoulam Declaration ¶ 9 and 10.

The obviousness rejection over Kloog is also reversed.

37 C.F.R. 41.50(b)

We enter the following new grounds of rejection in the present application.

1. Claims 1-6 and 8-24 are rejected under 35 U.S.C. § 102(b) and/or §103 over Brewster in view of Appellants' Admission.

2. Claims 1-6 and 8-24 are rejected under 35 U.S.C. §102(a) and/or §103 over Knoller in view of Appellants' Admission.

3. Claims 1-6 and 8-24 are rejected under 35 U.S.C. §135(b) over Claim 1 of Mechoulam.

4. Claims 1-6 and 8-24 are rejected under 35 U.S.C. §102(g)(2) as the claimed invention was made in this country by another inventor.

The rationale for these rejections is set forth below.

35 U.S.C. § 102 and/or §103

Claims 1-6 and 8-24 are rejected under 35 U.S.C. § 102(b) and/or §103 over Brewster as evidenced by Appellants' Admission in the specification, pages 36 and 39.

Brewster reports the results of a phase I clinical trial using dexanabinol of high enantiomeric purity. Brewster page 362, column 1. The dexanabinol used in the study was formulated in Cremaphor ethanol by Pharmos Corp., the assignee of the present application. Brewster, page 362, column 1. Appellants admit in the specification that the dexanabinol used in the Phase I study was "of high enantiomeric purity." Specification, page 36, line 32; page 39, line 22. In the Phase I study, "no psychomimetic side effects were detected." Brewster, page 364, column 2.

It appears that the high enantiomeric compound claimed was administered in the Phase I clinical study as "no psychomimetic side effects were detected." Brewster, page 364, column 2. Thus, Brewster anticipates claims 1-6, directed to various and similar enantiomeric excess compounds of dexanabinol as claim 1. With respect to claims 8-17, see Brewster, page 362, column 1, describing dexanabinol in Cremaphor-ethanol (65:35) in addition to EDTA[1], dl-α-tocopherol and saline. With respect to claims 18-20, see Brewster, page 363, describing specific dosing and intravenous and parenteral dosage forms of dexanabinol. Regarding claims 21-24, see Brewster, page 361-362, describing administration and subsequent neuroprotective effects of dexanabinol.

In the alternative, the claims are rejected under 35 U.S.C. §103 for obviousness over Brewster. Even if Brewster does not disclose some of the additional components in various of the dependent claims, such components would reasonably appear to be

[1] Ethylendiaminetetraacetic acid.

conventional pharmaceutical additives or forms of administration and do not distinguish the claimed compositions from those disclosed in Brewster, and which would have been obvious to one of ordinary skill in the art.

35 U.S.C. §102 and/or §103

Claims 1-6 and 8-24 are rejected under 35 U.S.C. §102(a) and/or §103 over Knoller.

Knoller reports the results of a phase II clinical trial using dexanabinol of high enantiomeric purity. Specification, page 34, lines 1-8; page 40, line 10; page 41, lines 15-16; and page 42, lines 4-11. The dexanabinol used in the study was formulated in Cremaphor[2] ethanol by Pharmos Corp., the assignee of the present application. Knoller, page 548, column 3. Thus, Knoller anticipates claims 1-6, directed to various and similar enantiomeric excess compounds of dexanabinol as claim 1. With respect to claims 8-17, see Knoller, page 548, column 2, describing dexanabinol in Cremaphor-ethanol. With respect to claims 18-20, see Knoller, page 548, describing specific dosing in identical glass vials and intravenous dosage forms of dexanabinol. Regarding claims 21-24, see Knoller, page 548 and 551, describing administration and subsequent neuroprotective effects of dexanabinol.

In the alternative, the claims are rejected under 35 U.S.C. §103 for obviousness over Knoller. Even if Knoller does not disclose some of the additional components in

[2] According to the specification, page 28, Cremaphor EL ® comprises polyoxyl 35 castor oil; 65% w/v with a cosolvent of edetic acid and vitamin E (tocopherol).

various of the dependent claims, such components would reasonably appear to be conventional pharmaceutical additives or forms of administration and do not distinguish the claimed compositions from those disclosed in Knoller, and which would have been obvious to one of ordinary skill in the art.

For each of the above anticipation rejections Appellants' burden under the circumstances presented herein is described in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

Therefore, should appellants argue that the Pharmos dexanabinol compounds used in either the Brewster Phase I clinical trial or the Knoller Phase II clinical trial are not identical or substantially identical to the claimed dexanabinol, appellants have the burden of proving that the prior art Pharmos products described in Brewster and Knoller do not necessarily or inherently possess the characteristics of this claimed product.

35 U.S.C. § 135(b)

Claims 1-6 and 8-24 are rejected under 35 U.S.C.§135(b)(1) over Claim 1 of Mechoulam.

35 U.S.C. § 135(b)(1) states in relevant part:

> (b) (1) A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted.

The invention of Mechoulam claim 1 is the same or substantially the same subject matter as Claim 1 of the present application. The claim language "essentially free of the (3R,4R) enantiomer" in claim 1 of Mechoulam encompasses the compound of claim 1 of the present application. In particular, see Mechoulam, column 3, compound II(a) and column 8, compound II(a), which is encompassed by the formula of Mechoulam claim 1, wherein R is a branched alkyl group having 9 carbon atoms. Compound II(a) of Mechoulam is characterized at column 3, lines 56 and 59, as having "absolute enantiomeric purity".

Thus, Mechoulam describes substantially the same subject matter claimed. Instant claims 1-3 are substantially the same as Mechoulam's claim 1. Claims 4-6 are substantially the same as Mechoulam's claim 2. Instant claims 8-20 are substantially the same as Mechoulam's claim 10, as the dosage forms and carriers are conventional in the art. Instant claims 21-23 are substantially the same as Mechoulam's claim 4, and claim 24 of the present application is substantially the same as Mechoulam's claim 8. In particular regard to claim 24, the specification describes that neuroprotective properties

of dexanabinol render it useful for the treatment of neurological disorders including head trauma and that by virtue of its analgesic properties dexanabinol is useful for the treatment of pain. Specification, p. 10.

Appellants now claim dexanabinol being in enantiomeric excess of at least 99.90% over the (3R,4R) enantiomer, i.e., which is essentially free of the (3R,4R) enantiomer, more than 1 year from the date in which the Mechoulam patent was granted on October 24, 1989. Such a claim is not permitted more than one year from the date on which the Mechoulam patent was granted.

35 U.S.C 102(g)(2)

Claims 1-6 and 8-24 are rejected under 35 U.S.C. §102(g)(2) as the claimed invention was made in this country by another inventor.

35 U.S.C. § 102(g)(2) states that:

> A person shall be entitled to a patent unless ... before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

The Mechoulam patent and the invention described therein has a constructive reduction to practice date of October 26, 1987, the date of the filing of the Mechoulam patent. As indicated in the above rejection of the claims under 35

U.S.C. § 135(b)(1), the dexanabinol compound, pharmaceutical compositions, and methods are the same or substantially the same as the compound, compositions and methods claimed by Mechoulam.

Thus, Mechoulam made the products and methods of the instant claims prior to Appellants, and thus appellants are not entitled to a patent under 35 U.S.C. § 102(g)(2).

CONCLUSION

The rejection of claims 1-10, 15-16 and 18-24 under 35 U.S.C. § 102(b) over Kloog is reversed. The rejection of claims 1-6 and 8-24 under 35 U.S.C. § 103(a) over Kloog is reversed.

This application contains four new grounds of rejection of the pending claims to be addressed by appellants.

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

REVERSED, 37 C.F.R. § 41.50(b)

Demetra J. Mills
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

Nancy J. Linck
Administrative Patent Judge

) BOARD OF PATENT
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